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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/600,125	04/10/2002	R.C. Warrington	10242-32	7782

1059 7590 04/10/2003

BERESKIN AND PARR
SCOTIA PLAZA
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TORONTO, ON M5H 3Y2
CANADA

EXAMINER
KRASS, FREDERICK F

ART UNIT	PAPER NUMBER
1614	12

DATE MAILED: 04/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/600,125	Warrington et al.
Examiner	**Art Unit**
Frederick Krass	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 52-80 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 52-80 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2.5
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Priority Claim

In order to perfect the claims for priority under Sections 371 and 119(e), it will be necessary for Applicant to amend the first line of the specification to refer particularly to the specific documents being relied upon.

Scope of Enablement

The following a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 52-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of 1) R-2HPA, R-2HMP or deprenyl in combination with 2) histidinol or cisplatinum, respectively to increase activity and/or treat cancer, does not reasonably provide enablement for the use of proparglyamines in combination with "antineoplastic agents" generally. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure

would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence or absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth hereinbelow.

1. The nature of the invention, state of the prior art, relative skill of those in the art, and the predictability of the art

The claimed invention relates to the treatment of cancer.

The relative skill of those in the art is generally that of a PHD candidate or PHD.

USP 6,465,448 represents a standard publication in the art and as such is directed to those having ordinary skill in the art. This publication demonstrates the unpredictability of the claimed subject matter. See specifically the disclosure at column 1, lines 56-60, which clearly teaches that the effects of combining anticancer agents cannot be predicted *a priori*, and must instead be determined empirically on a case-by-case basis for each particular drug combination.

Given the above facts, it is clear that the art to which the instant invention relates involves a relatively high degree of unpredictability.

2. The breadth of the claims

Claims 52-80 are broad and inclusive of many combinations of propargylamines and antineoplastic agents, with no claim specifically reciting a combination of 1) R-2HPA, R-2HMP, and 2) histidinol or cisplatinum. Furthermore, no specific cancer types are recited. The skilled artisan will appreciate that success in treating one type of cancer, e.g. colon cancer, does not provide an expectation of success for other unrelated types of cancer, e.g. brain cancer.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for using propargylamines to increase the activity of antineoplastic agents or to treat cancer, other than the use of 1) R-2HPA, R-2HMP or deprenyl in combination with 2) histidinol or cisplatinum, which are the only specific combinations actually tested in the working examples (see pages 14-16 of the instant specification).

4. The quantity of experimentation necessary

Applicant fails to provide guidance and information sufficient to allow the skilled artisan to ascertain which specific combinations of propargylamines and antineoplastic agents, known or to be discovered, can reasonably be expected to exhibit increased activity or to treat cancer without resorting to undue experimentation, other than the combination of 1) R-2HPA, R-2HMP or deprenyl and of 2) histidinol or cisplatinum. Testing would have to be conducted on each particular propargylamine and antineoplastic agent, across a variety of representative cancer types, with no expectation of success being present prior to testing.

Anticipation Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 52-56, 62, 64, 66-71, 77 and 78 are rejected under 35 U.S.C. 102(e) as being anticipated by Bobotas (USP 6,239,181).

The prior art discloses the use of selegiline (a.k.a. R(-)deprenyl – see the last paragraph of column 3) to protect peripheral nerve cells from the cytotoxic effects of antineoplastic agents including vincristine, vinblastine, cisplatin, paclitaxel, procarbazine, and 5-fluorouracil (column 5, lines 45-54, and working examples 1-4).

Regarding claims 53 and 54, the prior art does not specifically disclose increasing tumor sensitivity, which is useful in treating drug-resistant tumors. The prior art does, however, administer the same combination of active agents for the same utility (to protect normal cells from damage by anticancer agents), at comparable dosage levels (see and compare column 3, lines 38 and 39 of the prior art with page 12, lines 2 and 3 of the instant specification, keeping in mind that deprenyl is aromatic, so the prior

art dosages are increased ten-fold), and thus increased drug sensitivity (and by implication reduced drug-resistance) would be an inherent feature of the prior methods.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 59, 63, 74 and 79 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bobotas.

The prior art has been discussed in the "Anticipation" section above and differs from the instant claims insofar as the specific compound it discloses (deprenyl) has a methyl-substituted amino group, i.e. it corresponds to the instantly claimed compounds where "y" is one. The instantly claimed compounds, exemplified by the deprenyl homolog desmethyldeprenyl (see for example instant claim 63), have a value for "y" of zero.

Compounds which are homologs are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds will possess similar properties. See M.P.E.P. 2144.09. Accordingly, it would have been obvious to have used desmethyldeprenyl in place of its homolog, deprenyl, in protecting peripheral

nerves from the cytotoxic effects of antineoplastic agents as disclosed by Bobotas, motivated by the presumption of similar properties which arises from the close structural similarity of the compounds involved.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick Krass whose telephone number is (703) 308-4335. The examiner can normally be reached on Monday, Tuesday and Thursday from 9am to 5pm, and on Friday from 11am to 7pm. The examiner is off Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached at (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0193.

Frederick Krass
Primary Examiner
Art Unit 1614